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L6: Entry 1 of 29

File: USPT

Jul 31, 2001

US-PAT-NO: 6267958

DOCUMENT-IDENTIFIER: US 6267958 B1

TITLE: Protein formulation

DATE-ISSUED: July 31, 2001

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US-CL-CURRENT: 424/130.1, 424/138.1, 424/141.1, 424/143.1, 424/145.1, 424/155.1, 435/810, 514/2,
530/350, 530/387.1, 530/387.7, 530/388.1, 530/388.22, 530/388.8

CLAIMS:

What is claimed is:

1. A stable isotonic reconstituted formulation comprising an antibody in an amount of about 50 mg/mL to about 400 mg/mL and a diluent, which reconstituted formulation has been prepared from a lyophilized mixture of the antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole of antibody, and wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture before lyophilization.
2. The formulation of claim 1 wherein the lyoprotectant is sucrose.
3. The formulation of claim 1 wherein the lyoprotectant is trehalose.
4. The formulation of claim 1 which further comprises a buffer.
5. The formulation of claim 4 wherein the buffer is histidine or succinate.
6. The formulation of claim 1 which farther comprises a surfactant.

7. The formulation of claim 1 which is sterile.
8. A stable reconstituted formulation comprising an antibody in an amount of about 50 mg/mL to about 400 mg/mL and a diluent, which reconstituted formulation has been prepared from a lyophilized mixture of an antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole of antibody, and wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture before lyophilization.
9. The formulation of claim 8 wherein the antibody is an anti-IgE antibody.
10. The formulation of claim 8 wherein the antibody is an anti-HER2 antibody.
11. The formulation of claim 8 wherein the antibody is a full length humanized antibody.
12. The formulation of claim 8 which is isotonic.
13. A method for preparing a stable isotonic reconstituted formulation comprising reconstituting a lyophilized mixture of an antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole of antibody in a diluent such that the antibody concentration in the reconstituted formulation is at least 50 mg/mL, wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture before lyophilization.
14. The method of claim 13 wherein the lyoprotectant is sucrose.
15. The method of claim 13 wherein the lyoprotectant is trehalose.
16. The method of claim 13 wherein the lyophilized mixture further comprises a bulking agent which is added in an amount which adds mass to the lyophilized mixture and contributes to the physical structure of the lyophilized cake.
17. A method for preparing a formulation comprising the steps of:
 - (a) lyophilizing a mixture of an antibody and a lyoprotecting amount of a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole of antibody; and
 - (b) reconstituting the lyophilized mixture of step (a) in a diluent such that the reconstituted formulation is isotonic and stable and has an antibody concentration of about 80 mg/mL to about 400 mg/mL.
18. The method of claim 17 wherein the protein concentration in the reconstituted formulation is from about 80 mg/mL to about 300 mg/mL.
19. The method of claim 17 wherein the protein concentration in the reconstituted formulation is about 2-40 times greater than the protein concentration in the mixture before lyophilization.
20. The method of claim 17 wherein lyophilization is performed at a shelf temperature maintained at about 15-30.degree. C. throughout the entire lyophilization process.
21. An article of manufacture comprising:
 - (a) a container which holds a lyophilized mixture of an antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant: antibody is about 100-510 mole lyoprotectant:1 mole of antibody; and
 - (b) instructions for reconstituting the lyophilized mixture with a diluent to an antibody concentration in the reconstituted formulation of about 80 mg/mL to about 400 mg/mL.
22. The article of manufacture of claim 21 wherein the protein concentration in the reconstituted formulation is about 2-40 times greater than the protein concentration in the mixture before lyophilization.
23. The article of manufacture of claim 21 further comprising a second container which holds a diluent.
24. The article of manufacture of claim 23 wherein the diluent is bacteriostatic water for injection

(BWFI) comprising an aromatic alcohol.

25. A formulation comprising a lyophilized mixture of an antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole antibody.

26. A formulation comprising anti-HER2 antibody in amount from about 5-40 mg/mL, sucrose or trehalose in an amount from about 10-100 mM, a buffer and a surfactant.

27. The formulation of claim 26 further comprising a bulking agent which adds mass to the lyophilized mixture and contributes to the physical structure of the lyophilized cake.

28. The formulation of claim 27 wherein the bulking agent is mannitol or glycine.

29. The formulation of claim 26 which is lyophilized and stable at 30.degree. C. for at least 6 months.

30. The formulation of claim 29 which is reconstituted with a diluent such that the anti-HER2 antibody concentration in the reconstituted formulation is from about 10-30 mg/mL, wherein the reconstituted formulation is stable at 2-8.degree. C. for at least about 30 days.

31. The formulation of claim 30 wherein the diluent is bacteriostatic water for injection (BWFI) comprising an aromatic alcohol.

32. A formulation comprising anti-IgE antibody in amount from about 5-40 mg/mL, sucrose or trehalose in an amount from about 80-300 mM, a buffer and a surfactant.

33. The formulation of claim 32 which is lyophilized and stable at about 30.degree. C. for at least 1 year.

34. The formulation of claim 1 wherein the antibody in the formulation is a monoclonal antibody.

35. The formulation of claim 1 wherein the reconstituted formulation fails to display significant or unacceptable levels of chemical or physical instability of the antibody upon storage at 2-8.degree. C. for at least 30 days.

36. The formulation of claim 1 wherein less than about 10% of the antibody is present as an aggregate in the reconstituted formulation.

37. The formulation of claim 1 wherein less than about 5% of the antibody is present as an aggregate in the reconstituted formulation.

38. The formulation of claim 1 wherein the lyoprotectant is a non-reducing sugar.

39. The formulation of claim 1 wherein the lyoprotectant is a disaccharide.

40. The formulation of claim 39 wherein the lyoprotectant is a non-reducing disaccharide.

41. The formulation of claim 1 wherein the molar ratio of lyoprotectant:antibody is about 200-510 mole lyoprotectant:1 mole of antibody.

42. The article of manufacture of claim 23 wherein the diluent is sterile water.

43. The article of manufacture of claim 23 wherein the diluent is sterile saline solution.

44. The formulation of claim 25 wherein the antibody is a monoclonal antibody.

45. The formulation of claim 44 wherein the lyoprotectant is sucrose.

46. The formulation of claim 44 wherein the lyoprotectant is trehalose.

47. A stable reconstituted formulation comprising a monoclonal antibody in an amount of about 50 mg/mL to about 400 mg/mL and a diluent, which reconstituted formulation has been prepared from a lyophilized mixture of the monoclonal antibody and a sugar selected from the group consisting of sucrose and trehalose, wherein the molar ratio of sugar:monoclonal antibody is about 100-510 mole sugar:1 mole of monoclonal antibody, and wherein the monoclonal antibody concentration in the reconstituted formulation is about 2-40 times greater than the monoclonal antibody concentration in the mixture before lyophilization.

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Search Results - Record(s) 1 through 10 of 17 returned.

☐ **1. Document ID: US 6267958 B1**

L9: Entry 1 of 17

File: USPT

Jul 31, 2001

DOCUMENT-IDENTIFIER: US 6267958 B1

TITLE: Protein formulation

CLPR:

1. A stable isotonic reconstituted formulation comprising an antibody in an amount of about 50 mg/mL to about 400 mg/mL and a diluent, which reconstituted formulation has been prepared from a lyophilized mixture of the antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole of antibody, and wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture before lyophilization.

CLPR:

6. The formulation of claim 1 which farther comprises a surfactant.

CLPR:

8. A stable reconstituted formulation comprising an antibody in an amount of about 50 mg/mL to about 400 mg/mL and a diluent, which reconstituted formulation has been prepared from a lyophilized mixture of an antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole of antibody, and wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture before lyophilization.

CLPR:

13. A method for preparing a stable isotonic reconstituted formulation comprising reconstituting a lyophilized mixture of an antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole of antibody in a diluent such that the antibody concentration in the reconstituted formulation is at least 50 mg/mL, wherein the antibody concentration in the reconstituted formulation is about 2-40 times greater than the antibody concentration in the mixture before lyophilization.

CLPR:

mg/mL to about 400 mg/mL and a diluent, which reconstituted formulation has been prepared from a lyophilized mixture of the monoclonal antibody and a sugar selected from the group consisting of sucrose and trehalose, wherein the molar ratio of sugar:monoclonal antibody is about 100-510 mole sugar:1 mole of monoclonal antibody, and wherein the monoclonal antibody concentration in the reconstituted formulation is about 2-40 times greater than the monoclonal antibody concentration in the mixture before lyophilization.

CLPV:

(a) lyophilizing a mixture of an antibody and a lyoprotecting amount of a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole of antibody; and

CLPV:

(b) reconstituting the lyophilized mixture of step (a) in a diluent such that the reconstituted formulation is isotonic and stable and has an antibody concentration of about 80 mg/mL to about 400 mg/mL.

CLPV:

(a) a container which holds a lyophilized mixture of an antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant: antibody is about 100-510 mole lyoprotectant:1 mole of antibody; and

CLPV:

(b) instructions for reconstituting the lyophilized mixture with a diluent to an antibody concentration in the reconstituted formulation of about 80 mg/mL to about 400 mg/mL.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	FIGS	Draw Desc	Image
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☐ 2. Document ID: US 6187572 B1

L9: Entry 2 of 17

File: USPT

Feb 13, 2001

DOCUMENT-IDENTIFIER: US 6187572 B1

TITLE: Method of inactivation of viral and bacterial blood contaminants

CLPR:

16. The process according to claim 15 wherein said hybridoma cell lines produce monoclonal antibodies.

CLPR:

42. The process according to claim 1 further comprising the step of treating said composition with organic solvents or detergents.

CLPR:

44. The process according to claim 42 wherein said detergent is "Tween" 80.

CLPR:

45. The process according to claim 42 wherein said detergent is a nonionic detergent.

CLPR:

46. The process according to claim 1 wherein said freeze-dried solid has a residual moisture content of 10% or less.

CLPR:

58. The composition according to claim 55 comprising frozen or freeze-dried cell culture or a component of a cell culture.

CLPV:

(ii) freezing or freeze-drying said composition and sensitizer mixture; and

CLPV:

(iii) exposing said frozen or freeze-dried composition and sensitizer mixture to electromagnetic radiation selected from the group consisting of visible, UV, x-ray, and gamma radiation of sufficient wavelength and intensity for a period of time sufficient to activate said sensitizer whereby the activation of said sensitizer reduces said contamination in said composition.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWC	Draw. Desc	Image
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☐ 3. Document ID: US 5932428 A

L9: Entry 3 of 17

File: USPT

Aug 3, 1999

DOCUMENT-IDENTIFIER: US 5932428 A

TITLE: Method for preparing a sample in a scan capillary for immunofluorescent interrogation

CLPR:

15. The method of claim 1, wherein the adding a reagent step includes adding a detergent to the sample.

CLPR:

18. The method of claim 1, wherein the adding a reagent step includes adding a dried reagent that does not substantially affect an initial volume of the sample.

CLPR:

28. The method of claim 22, wherein the fluorescent compound is a cyanine dye bound to a monoclonal antibody.

CLPR:

39. The sample preparation of claim 37, wherein the reagent is a detergent.

Full	Title	Citation	Front	Review	Classification	Date	Reference
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☐ 4. Document ID: US 5759864 A

L9: Entry 4 of 17

File: USPT

Jun 2, 1998

DOCUMENT-IDENTIFIER: US 5759864 A

TITLE: Methods for reducing background binding in antibody preparations

CLPR:

5. The method according to claim 1, wherein said nonionic surfactant is selected from a polyethoxylated alcohols, polyethoxylated alkylphenol, polyethoxylated fatty acid, polyalkylene oxide block copolymer, carboxylic acid ester, carboxylic amide, or combinations of any two or more thereof.

CLPR:

16. The method according to claim 1, wherein said antibody preparation is polyclonal.

CLPR:

17. The method according to claim 16, wherein said polyclonal antibody is raised against luciferase.

CLPR:

18. The method according to claim 16, wherein said polyclonal antibody is raised in an animal selected from rabbit, rat, mouse, goat, sheep, chicken, horse, donkey, or guinea pig.

CLPR:

21. The method according to claim 1, wherein said permeabilized cells are lyophilized prior to treating said antibody preparation.

CLPR:

29. The method according to claim 28, wherein said antibody preparation is treated with said lyophilized, permeabilized, and optionally immobilized cells for a period ranging from about 30 minutes to about 24 hours at a temperature ranging from about 4.degree. C. to about 37.degree. C.

CLPR:

30. The method according to claim 28, wherein said antibody preparation is treated with said lyophilized, permeabilized, and optionally immobilized cells for a period ranging from about 30 minutes to about 5 hours at a temperature ranging from about 22.degree. C. to about 37.degree. C.

CLPR:

31. The method according to claim 28, wherein said antibody preparation is treated with said lyophilized, permeabilized, and optionally immobilized cells for a period ranging from about 30 minutes to about 1 hour at a temperature ranging from about 22.degree. C. to about 37.degree. C.

CLPR:

32. A treated anti-luciferase polyclonal antibody preparation prepared according to the method of claim 1, wherein said treated anti-luciferase polyclonal antibody preparation is substantially free of background binding due to intracellular proteins.

CLPR:

33. An anti-luciferase polyclonal antibody preparation, wherein said anti-luciferase polyclonal antibody preparation is substantially free of background binding due to intracellular protein(s).

CLPR:

34. A reagent comprising immobilized, lyophilized, permeabilized whole cells, wherein the intracellular protein(s) of said cells are not substantially denatured, and wherein said whole cells are from a vertebrate species.

CLPV:

(iii) lyophilizing the permeabilized, and optionally immobilized whole cells;

CLPV:

(iv) treating said antibody preparation with said lyophilized, permeabilized, and optionally immobilized whole cells to produce a treated antibody preparation; then

CLPV:

(v) separating said treated antibody preparation from said lyophilized, permeabilized, and optionally immobilized whole cells.

CLPW:

wherein said permeabilizing agent comprises an agent selected from the group consisting of alcohols and aqueous alcohols, aldehydes and aqueous aldehydes, ketones and aqueous ketones, nonionic surfactants and aqueous media containing nonionic surfactants, and combinations of any two or more thereof, provided, however, that the permeabilizing agent is not neat acetone; then

CLPW:

wherein said permeabilizing agent comprises an agent selected from the group consisting of alcohols and aqueous alcohols, aldehydes and aqueous aldehydes, ketones and aqueous ketones, nonionic surfactants and aqueous media containing nonionic surfactants, and combinations of any two or more thereof, provided, however, that the permeabilizing agent is not neat acetone;

Full	Title	Citation	Front	Review	Classification	Date	Reference
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☐ 5. Document ID: US 5759774 A

L9: Entry 5 of 17

File: USPT

Jun 2, 1998

DOCUMENT-IDENTIFIER: US 5759774 A

TITLE: Method of detecting circulating antibody types using dried or lyophilized cells

CLPR:

5. A method according to claim 3 or 4 wherein, prior to said reconstituting of material in step (d) the dried or lyophilized material from step (c) is stored.

CLPR:

8. A method according any of claim 3, 4, 6 or 7 wherein said sample is selected from the group consisting of plasma, serum, antiserum, hybridoma fluid, tissue or body fluids, cell culture fluids, whole blood, and fractions derived from tissue or body fluids, cell culture fluids, whole blood, plasma, serum, antiserum, or hybridoma fluid.

CLPR:

25. A method according to claim 6 or 7 wherein said lyophilized or dried composition further comprises an enhancer for enhancing a desired ligand-receptor reaction.

CLPR:

52. A method according to claim 51 wherein said antibodies are derived from polyclonal antisera.

CLPR:

57. A method according to any of claims 1, 2, 3 or 4 wherein a plurality of separate compositions is lyophilized-or dried while attached to a solid support, thereby providing a panel of standard compositions for screening a predetermined set of antibody types.

CLPR:

64. A method according to claim 57 wherein said sample composition is animal antisera.

CLPR:

84. A method according to claim 83 wherein said immunoglobulin-binding protein is selected from recombinant proteins, polyclonal antibodies, and monoclonal antibodies.

CLPR:

107. A diagnostic panel comprising a plurality of compartments or sectors, each containing a different lyophilized material selected from the group consisting of cell, cell membrane, lymphocytes, platelets, peripheral blood cells, stem cells, liposomes, hemosomes, cell membrane ghost, cultured mammalian cells, stroma, hybridoma cells or erythrocytes, lyophilized or dried in the presence of a cryoprotectant comprising a monosaccharide, disaccharide or trisaccharide and at least one biologically compatible amphipathic polymer, and known to have one or more antigens which are recognized and bound by a selected antibody type.

CLPR:

120. A panel according to claim 116 wherein said antibodies are selected from the group consisting of polyclonal antibodies and monoclonal antibodies.

CLPR:

135. A panel according to claim 134 wherein said material is subjected to said treatments prior to attachment to a solid support and lyophilization.

CLPR:

136. A panel according to claim 134 wherein said material is subjected to said treatments after attachment to a solid support, lyophilization, and rehydration.

CLPR:

137. A panel according to claim 134 wherein said treatments comprise exposure to an agent selected from the group consisting of proteolytic enzymes, detergents, chemical fixatives, low ionic strength saline, high ionic strength saline, and high molecular weight polymer solutions.

CLPR:

152. A diagnostic kit for detecting in vitro the presence or absence of a predetermined circulating antibody-type in a plasma or serum sample, said kit comprising a panel of a plurality of compartments, each of said compartments containing a different lyophilized material selected from the group consisting of cells lymphocytes, platelets, peripheral blood cells, stem cells, liposomes, hemosomes, cell membrane ghost, cultured mammalian cells, stroma, hybridoma cells or erythrocytes, lyophilized or dried in the presence of a cryoprotectant comprising a monosaccharide, disaccharide or trisaccharide and at least one biologically compatible amphipathic polymer and wherein each lyophilized material is characterized by one or more antigens which are recognized and bound by a predetermined antibody-type.

CLPR:

162. A kit according to claim 152 wherein said lyophilized material is selected from the group consisting of beads, pellets and droplets, and said compartments comprise blister packs accommodating said material.

CLPV:

c lyophilizing said bound material and cryoprotective medium to form a lyophilized composition.

CLPV:

c evaporatively drying said bound material and cryoprotective medium to form a dried composition.

CLPV:

c lyophilizing said bound material and cryoprotective medium;

CLPV:

(d) reconstituting the lyophilized material;

CLPV:

(d) reconstituting the dried material;

CLPV:

(a) reconstituting a lyophilized composition, said composition comprising a material selected from the group consisting of cells, cell membranes, lymphocytes, platelets, peripheral blood cells, stem cells, liposomes, hemosomes, cell membrane ghosts, cultured mammalian cells, stroma, hybridoma cells and erythrocytes lyophilized or dried in the presence of a cryoprotectant comprising a monosaccharide, a disaccharide or a trisaccharide and at least one biologically compatible amphipathic polymer and known to have a profile of cytosolic or cell surface receptors which are recognized and bound by said ligand;

CLPV:

(a) reconstituting a dried composition, said composition comprising a material selected from the group consisting of cells, cell membranes, lymphocytes, platelets, peripheral blood cells, stem cells, liposomes, hemosomes, cell membrane ghosts, cultured mammalian cells, stroma, hybridoma cells and erythrocytes lyophilized or dried in the presence of a cryoprotectant comprising a monosaccharide, a disaccharide or a trisaccharide and at least one biologically compatible amphipathic polymer and known to have a profile of cytosolic or cell surface receptors which are recognized and bound by said ligand;

Full	Title	Citation	Front	Review	Classification	Date	Reference
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☐ 6. Document ID: US 5733572 A

L9: Entry 6 of 17

File: USPT

Mar 31, 1998

DOCUMENT-IDENTIFIER: US 5733572 A

TITLE: Gas and gaseous precursor filled microspheres as topical and subcutaneous delivery vehicles

CLPR:

15. A composition according to claim 12 wherein the synthetic polymer is selected from the group consisting of polyethylenes, polypropylenes, polyurethanes, polyamides, polystyrene, polylactic acids, fluorinated hydrocarbons, fluorinated carbons, and polymethylmethacrylate.

CLPR:

18. A composition according to claim 17 wherein the ingestible oils are selected from the group consisting of peanut oil, canola oil, olive oil, safflower oil, and corn oil; wherein compounds for the mixed micelle systems are selected from lauryltrimethylammonium bromide, cetyltrimethylammonium bromide, myristyltrimethylammonium bromide, alkyldimethylbenzylammonium chloride (alkyl=C.sub.12,C.sub.14,C.sub.16.), benzyldimethyldodecylammonium bromide/chloride, benzyldimethyl hexadecylammonium bromide/chloride, benzyl-dimethyltetradecylammonium bromide/chloride, cetyldimethylethylammonium bromide/chloride, and cetylpyridinium bromide/chloride; wherein the viscosity modifiers are selected from the group consisting of carbohydrates, polyethers having a

molecular weight in the range of between 400 and 100,000, di- and trihydroxy alkanes and their polymers having a molecular weight in the range of between 200 and 50,000; wherein the emulsifying and/or solubilizing agents are selected from the group consisting of acacia, cholesterol, diethanolamine, glyceryl monostearate, lanolin alcohols, lecithin, mono- and di-glycerides, mono-ethanolamine, oleic acid, oleyl alcohol, poloxamer, polyoxyethylene 50 stearate, polyoxyl 35 castor oil, polyoxyl 10 oleyl ether, polyoxyl 20 cetostearyl ether, polyoxyl 40 stearate, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, propylene glycol diacetate, propylene glycol monostearate, sodium lauryl sulfate, sodium stearate, sorbitan mono-laurate, sorbitan mono-oleate, sorbitan mono-palmitate, sorbitan monostearate, stearic acid, trolamine, and emulsifying wax; wherein the suspending and/or viscosity-increasing agents are selected from the group consisting of acacia, agar, alginic acid, aluminum monostearate, bentonite, purified bentonite, magma bentonite, carbomer 934P, carboxymethylcellulose calcium, carboxymethylcellulose sodium 12, carboxymethylcellulose sodium, carrageenan, microcrystalline cellulose, dextran, gelatin, guar gum, veegum, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, magnesium-aluminum-silicate, methylcellulose, pectin, polyethylene oxide, polyvinyl alcohol, povidone, propylene glycol alginate, silicon dioxide, silicon dioxide, colloidal, zinc oxide, sodium alginate tragacanth, xanthan gum, .alpha.-d-gluconolactone, glycerol and mannitol; wherein the synthetic suspending agents are selected from the group consisting of polyethyleneglycol, polyvinylpyrrolidone, polyvinylalcohol, polypropylene glycol, and polysorbate; and wherein the tonicity-raising agents are selected from the group consisting of sorbitol, propyleneglycol and glycerol.

CLPR:

50. A composition of claim 1 wherein said microsphere comprises a surfactant.

CLPR:

59. A composition of claim 50 wherein said microsphere is lyophilized.

CLPV:

(2) monoclonal antibodies;

CLPV:

(8) skin absorption enhancing agents selected from the group consisting of pyrrolidones, fatty acids, sulfoxides, amines, terpenes, terpenoids, surfactants, alcohols, urea, glycols, azone, n-alkanols, n-alkanes, orgelase, and alphaderm cream;

Full	Title	Citation	Front	Review	Classification	Date	Reference
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☐ 7. Document ID: US 5641865 A

L9: Entry 7 of 17

File: USPT

Jun 24, 1997

DOCUMENT-IDENTIFIER: US 5641865 A

TITLE: Interaction system comprising a surfactant-stabilized disperse aqueous phase containing an antibody or antibody fragment

CLPR:

1. An interaction system, including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, which comprises a surfactant-stabilized microheterogeneous dispersion of aqueous phase in a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or a water-immiscible super-critical fluid, said aqueous phase containing an amount of said monoclonal antibody or said monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the restrictive amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the organic from 15:1 to 40:1.

CLPR:

2. In a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or water-immiscible supercritical fluid, an interaction system including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, which comprises a plurality of surfactant-stabilized microheterogeneous disperse aqueous phase particles, said particles containing an amount of said monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination or at least two of the foregoing, and wherein the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 15:1 to 40:1.

CLPR:

3. An interaction system including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, which comprises a surfactant-stabilized dispersion of aqueous phase particles containing said monoclonal antibody or monoclonal antibody fragment in a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or a water-immiscible supercritical fluid, the aqueous phase particles being of size in the maximum dimension less than the wavelength of visible light such that the system is transparent to such light, and said aqueous phase particles containing an amount of said monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 15:1 to 40:1.

CLPR:

4. In a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or water-immiscible supercritical fluid, an interaction system including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, which comprises a plurality of surfactant-stabilized microheterogeneously dispersed aqueous phase particles, the aqueous phase particles being of size in the maximum dimension less than the wavelength of visible light, and said aqueous phase particles containing an amount of said monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective amounts of said aqueous solution and solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 15:1 to 40:1.

CLPR:

5. An interaction system including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest which comprises a surfactant-stabilized microemulsion of aqueous

phase, or a dispersion of surfactant-stabilized aqueous reverse micelles, in a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or a water-immiscible supercritical fluid, said aqueous phase or reverse micelles containing an amount of said monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 16:1 to 40:1.

CLPR:

6. In a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or a water-immiscible supercritical fluid, an interaction system including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, which comprises a plurality of surfactant-stabilized microemulsified aqueous phase particles, or a dispersion of surfactant-stabilized aqueous reverse micelles, containing an amount of said monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 15:1 to 40:1.

CLPR:

7. A method of forming an interaction system including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, which comprises the step of surfactant-stabilizing a microheterogeneous dispersion of aqueous phase in a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or a water-immiscible supercritical fluid, said aqueous phase containing an amount of said monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 15:1 to 40:1.

CLPR:

8. A method of forming an interaction system including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, which comprises the steps of combining an aqueous solution of said monoclonal antibody or monoclonal antibody fragment and a solution of a surfactant in a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or a water-immiscible supercritical fluid, and agitating the combination to form a surfactant-stabilized microheterogeneous dispersion of aqueous phase in said fluid, said surfactant being present in an amount sufficient to effect formation of said dispersion and containing an amount of monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 5:1 to 40:1.

CLPR:

9. A method of forming an interaction system including a monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, which comprises the step of injecting an aqueous solution of said monoclonal antibody or monoclonal antibody fragment into a solution of a surfactant in a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or

water-immiscible supercritical fluid, said surfactant being present in an amount sufficient to effect the formation of a surfactant-stabilized microheterogeneous dispersion of aqueous phase in said fluid, and said aqueous phase containing an amount of said monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 15:1 to 40:1.

CLPR:

10. A method as defined in claim 9, wherein the surfactant is sodium bi-(2-ethylhexyl)-sulfosuccinate and said ratio is in the range from 21:1 to 31:1.

CLPR:

11. A method of forming an interaction system, which comprises the steps of adding to a surfactant-stabilized microheterogeneous dispersion of aqueous phase in a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or a water-immiscible supercritical fluid, a freeze-dried monoclonal antibody or monoclonal antibody fragment capable of binding with a species of interest, in powder form, and mixing the protein powder with the microheterogeneous dispersion of aqueous phase in the fluid to form a microheterogeneous surfactant-stabilized dispersion of aqueous phase in the fluid, said aqueous phase containing said monoclonal antibody or monoclonal antibody fragment, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amount of water to surfactant is in the range from 15:1 to 40:1.

CLPR:

12. A method as defined in claim 11, wherein the surfactant is sodium bi-(2-ethylhexyl)-sulfosuccinate said ratio is in the range from 21:1 to 31:1.

CLPR:

13. A method of interacting a monoclonal antibody or monoclonal antibody fragment capable of binding with at least one species of interest, which comprises the step of maintaining a system comprising a surfactant-stabilized microheterogeneous dispersion of aqueous phase in a water-immiscible organic solvent, a mixture of water-immiscible organic solvents or a water-immiscible supercritical fluid, said aqueous phase containing an amount of said monoclonal antibody or monoclonal antibody fragment sufficient to effect said binding, at conditions under which the monoclonal antibody or monoclonal antibody fragment is accessible to the species and that are sufficient to effect said binding for a time sufficient for said binding to occur, wherein said surfactant is anionic, cationic, nonionic, amphoteric or a combination of at least two of the foregoing, and wherein the respective the respective amounts of said aqueous solution and said solution of surfactant in organic solvent or supercritical fluid are such that the molar ratio of the amounts of water to surfactant is in the range from 15:1 to 40:1.

Full	Title	Citation	Front	Review	Classification	Date	Reference
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□ 8. Document ID: US 5585246 A

L9: Entry 8 of 17

File: USPT

Dec 17, 1996

DOCUMENT-IDENTIFIER: US 5585246 A

TITLE: Method for preparing a sample in a scan capillary for immunofluorescent interrogation

CLPR:

17. The method of claim 2, wherein said reagent is a detergent.

CLPR:

20. The method of claim 2, wherein said reagent is a dried reagent that does not substantially affect an initial volume of the whole blood sample.

CLPR:

34. The method of claim 24, wherein said fluorescent compound is a cyanine dye bound to a monoclonal antibody.

CLPR:

43. The sample preparation of claim 37, wherein said reagent is a detergent.

Full	Title	Citation	Front	Review	Classification	Date	Reference
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☐ 9. Document ID: US 5532172 A

L9: Entry 9 of 17

File: USPT

Jul 2, 1996

DOCUMENT-IDENTIFIER: US 5532172 A

TITLE: Process and reagent for the determination of low density lipoproteins (LDL)

CLPR:

5. The method of claim 1, wherein said polyclonal antibodies are immobilized on a solid phase.

CLPR:

7. The method of claim 5, comprising separating said polyclonal antibodies immobilized on a solid phase, by centrifugation.

CLPR:

10. The reagent of claim 8, wherein said polyclonal antibodies are in immobilized form.

CLPR:

11. The reagent of claim 8, wherein said polyclonal antibodies are lyophilized.

CLPR:

12. The reagent of claim 8, wherein said polyclonal antibodies are in solution.

CLPR:

13. The reagent of claim 8, wherein said reagent which determines cholesterol contains cholesterol oxidase, cholesterol esterase, peroxidase, 3,4-dichlorophenol, phenol, 4-aminopehnazone, a non-ionic detergent, magnesium aspartate, and a buffer at a pH of from 7 to 8.5.

CLPR:

14. The reagent of claim 10, wherein said polyclonal antibodies are immobilized on a carrier substance selected from the group consisting of a polysaccharide, cellulose, dextran, starch, a starch derivative, a silicate, a polyamide, collagen latex, aluminum oxide, and bovine serum albumin.

CLPR:

15. The reagent of claim 10, wherein said polyclonal antibodies are immobilized on a surface of a synthetic resin test tube.

CLPV:

(a) adding to said body fluid sample polyclonal antibodies which bind to apolipoprotein A and to apolipoprotein E, wherein said polyclonal antibodies are obtained by immunizing a first animal with apolipoprotein A, and a second animal with apolipoprotein E and bind to and precipitate all of (i) high density lipoproteins, (ii) very low density lipoproteins, and (iii) chylomicrons in said body fluid sample when contacted thereto, but do not precipitate low density lipoproteins, under conditions favoring binding and precipitating all of (i), (ii), and (iii) present in said body fluid sample,

CLPV:

(ii) polyclonal antibodies which bind to and precipitate high density lipoproteins, very low density lipoproteins, and chylomicrons, but not low density lipoproteins.

Full	Title	Citation	Front	Review	Classification	Date	Reference
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□ 10. Document ID: US 5288502 A

L9: Entry 10 of 17

File: USPT

Feb 22, 1994

DOCUMENT-IDENTIFIER: US 5288502 A

TITLE: Preparation and uses of multi-phase microspheres

CLPR:

4. A delivery system for tumor necrosis factor with biodegradable multi-phase microspheres said microspheres comprising a lyophilized microemulsion of an aqueous solution of tumor necrosis factor in a fixed oil, and an essentially water insoluble, biodegradable polymeric matrix of polylactic acid or polylactic glycolic acid, wherein the polymeric matrix surrounds said microemulsion of tumor necrosis factor and fixed oil.

CLPR:

17. The delivery system of claim 4 or 6 wherein the microemulsion consists of lyophilized tumor necrosis factor in a fixed oil and the polymeric matrix is poly-lactic acid (PLGA).

CLPR:

38. The method of claim 29 wherein the microemulsion comprises about 1% w/w Tween 80 of the microemulsion.

CLPR:

43. The method of claim 29 wherein the molecular compound is unstable in water, and wherein the microemulsion is lyophilized prior to dispersing the microemulsion into the polymer solution to form a W/O/"W" emulsion.

CLPV:

monoclonal antibodies;

CLPV:

preparing a first mixture of a water-soluble drug in water, gelatin and Tween 80 to form an aqueous phase;

CLPV:

preparing a first mixture of a water-soluble protein, peptide, or dug in water, gelatin and Tween 80 to form an aqueous base;

Full	Title	Citation	Front	Review	Classification	Date	Reference
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16. The method of claim 13 wherein the lyophilized mixture further comprises a bulking agent which is added in an amount which adds mass to the lyophilized mixture and contributes to the physical structure of the lyophilized cake.

CLPR:

19. The method of claim 17 wherein the protein concentration in the reconstituted formulation is about 2-40 times greater than the protein concentration in the mixture before lyophilization.

CLPR:

20. The method of claim 17 wherein lyophilization is performed at a shelf temperature maintained at about 15-30.degree. C. throughout the entire lyophilization process.

CLPR:

22. The article of manufacture of claim 21 wherein the protein concentration in the reconstituted formulation is about 2-40 times greater than the protein concentration in the mixture before lyophilization.

CLPR:

25. A formulation comprising a lyophilized mixture of an antibody and a lyoprotectant which prevents or reduces chemical or physical instability of the antibody upon lyophilization and subsequent storage, wherein the molar ratio of lyoprotectant:antibody is about 100-510 mole lyoprotectant:1 mole antibody.

CLPR:

26. A formulation comprising anti-HER2 antibody in amount from about 5-40 mg/mL, sucrose or trehalose in an amount from about 10-100 mM, a buffer and a surfactant.

CLPR:

27. The formulation of claim 26 further comprising a bulking agent which adds mass to the lyophilized mixture and contributes to the physical structure of the lyophilized cake.

CLPR:

29. The formulation of claim 26 which is lyophilized and stable at 30.degree. C. for at least 6 months.

CLPR:

32. A formulation comprising anti-IgE antibody in amount from about 5-40 mg/ML, sucrose or trehalose in an amount from about 80-300 mM, a buffer and a surfactant.

CLPR:

33. The formulation of claim 32 which is lyophilized and stable at about 30.degree. C. for at least 1 year.

CLPR:

34. The formulation of claim 1 wherein the antibody in the formulation is a monoclonal antibody.

CLPR:

44. The formulation of claim 25 wherein the antibody is a monoclonal antibody.

CLPR:

47. A stable reconstituted formulation comprising a monoclonal antibody in an amount of about 50

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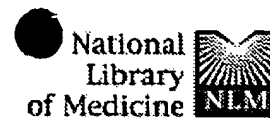
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